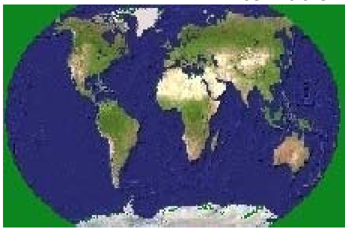

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A Study on the Rational Use of Antimicrobial Prophylaxis in Surgery

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Abstract
Irrational antibiotic use in surgical prophylaxis is of global concern due to the emergence of bacterial resistance and high healthcare costs. This study was done to compare the use of surgical antibiotic prophylaxis in a tertiary hospital with two international guidelines, American Society of Health-System Pharmacists (ASHP) and the Society of Thoracic Surgeons (STS) and the hospital antibiotic policy. A sample of 41 surgical patients was studied. The criteria used for comparison are the timing of the first dose of antibiotic, the choice and dosage of antibiotic used, intra-operative re-dosing and the duration of prophylaxis. The timing of the first prophylactic dose in 87% of the cases was as per the guidelines and the hospital antibiotic policy. The choice of antibiotic was right in 85.37% and 100% cases according to the ASHP and the STS guidelines, respectively. Continuous audits, physician education, providing written protocols and other interventions can improve the rationality of use of surgical antibiotic prophylaxis and conformance to the AHSP and STS guidelines.

Keywords: Antibiotic Policy, ALOS, ASHP, STS, Prophylaxis.

1. Introduction

Surgical antibiotic prophylaxis is given to almost all patients undergoing surgery to prevent the incidence of Surgical Site Infections (SSI). Surgical site infections, also called as surgical wound infections, are the second most common nosocomial infections next to urinary tract infections. Their occurrence in patients leads to increased mortality rates, readmission rates and increased healthcare costs. The basic principle of antibiotic prophylaxis in surgery is to reach adequate drug levels both in the serum as well as the wound tissue during the entire time the skin incision is open in the operating room. Adequate drug levels mean that the level must be more than the Minimum Inhibitory Concentration (MIC) of the commonly encountered microorganisms for each procedure. Antibiotic prophylaxis should be aimed to achieve this and just what is required to prevent infections post-operatively without changing the microbiological flora and susceptibility patterns in the hospital and the patient.

Development of resistance in bacteria has emerged as a global health issue and is due to prolonged, irrational and inappropriate antibiotic use. Inappropriate antibiotic use can arise from inappropriate choice of antibiotic or inappropriate dosing and must be balanced with the use for reduction of post-operative infections. Several studies have been conducted in different settings to establish an appropriate regimen for antibiotic prophylaxis in surgery. These have been used to formulate evidence-based guidelines for surgical antibiotic prophylaxis.

2. Materials and Methods

Development of resistance in bacteria and spiraling healthcare costs are associated often with irrational and prolonged use of antibiotic prophylaxis in surgery. A balance has to be made between the risk of surgical site infections and the emergence of resistance in microorganisms associated with the routine use of antibiotics in surgical prophylaxis. This study was conducted in order to evaluate the rationality of antibiotic use in prophylaxis for surgical procedures.

All surgical patients, both adult and paediatric were included. Patients who had recent infections, who were already receiving antibiotics at the time of surgery, who were undergoing emergency surgery or day care surgery and end-stage renal disease patients are excluded. The scope is limited to only the use of antibiotics in prophylaxis, that is, the prevention of an infection. Data was collected prospectively from each patient by direct observation and recorded in a pre-structured data collection form.

Data was collected such as the timing of antibiotic dose, the antibiotic choice used, duration and type of surgery, etc. Data was also collected from the medical records of the same patients. The data collected from the medical records includes demographic characteristics, past diseases, diagnosis, duration of prophylaxis and timing of last dose, length of stay, any drug allergies, infections, microbiological results, etc.

3. Results

Data was collected initially from 55 patients and 14 patients were excluded due to already being on antibiotic therapy at the time of the surgery. Hence, 41 patients form the sample in this study. Of these, 31 patients underwent cardiothoracic surgeries; out of which 18 patients underwent coronary artery bypass graft (CABG) surgeries. There were 7 paediatric surgeries, all for congenital heart diseases. There were 6 other adult cardiac surgeries. There were 10 non-cardiac surgeries.

Demographic details of the patients included in the sample are given in Table-1. This table shows the mean age in years of adult and paediatric patients and the gender distribution of the sample. Out of the 41 patients in the sample, 34 were adult patients and 7 were paediatric patients. There were 29 male patients and 12 female patients.

Table 1: Demographic Details of the Patients Included in the Sample.

Demographic Data	
Age in years (Mean ± SD)	43.94 ± 22.72
Adult Patients	52.38 ± 13.92
Pediatric Patients	2.93 ± 3.11
Gender (%) Male	29 (70.73%)
Female	12 (29.27%)
TOTAL	41

The demographic details of the initial group of 55 patients before the exclusion of 14 patients are given in table-2. In this initial group of 55 patients, there were 42 adult patients and 13 paediatric patients. There were 36 male patients and 19 female patients in the group.

Table 2: Demographic Details of the Initial Group of Patients

Demographic Data	
Age in years (Mean ± SD)	40.86 ± 24.94
Adult Patients	52.83 ± 13.99
Paediatric Patients	2.16 ± 2.62
Gender (%) Male	36 (65.45%)
Female	19 (34.55%)
TOTAL	55

Details of the pre-operative and post-operative antibiotic therapy in 8 of the 14 excluded patients are given in table-3. These patients were excluded because they were already receiving antibiotics at the time of surgery. Hence, they could not be given the routine surgical prophylaxis but were given a line of treatment in continuity with what was already being prescribed.

Table 3: Details of antibiotic therapy of patients excluded from sample.

Age/ Gender	*Surgery*	*Co-existing/recent infections*	*Pre-operative antibiotics*	*Duration*	*Post-operative antibiotics*	*Duration*
1 month 22 days / M	TOF repair and BT Shunt	Pharyngeal colonization with *Klebsiella pneumoniae*	Inj. Sulbactam/Cefoperazone 150 mg IV TID	48 hours	Inj. Sulbactam/Cefoperazone 120 mg IV TID	6 days
			Inj. Amikacin 60 mg IV OD	32 hours	Inj. Amikacin 40 mg IV OD	6 days 3 hours
62yrs/M	CABG with deroofing of AV groove abscess and debridement of necrotic RV epicardial tissue	RCA stent infection with AV groove abscess (sepsis with MODS, post-operatively)	Inj. Imipenem/Cilastatin 500mg IV QID	66 hours	Inj. Imipenem/Cilastatin 500mg IV QID	10 days 8 hours
			Inj. Vancomycin 1 gm IV BD	70 hours	Inj. Vancomycin 1 gm IV BD	66 hours
			Inj. Fluconazole 400 mg IV OD	48 hours	Inj. Fluconazole 400 mg IV OD	8 days
3yrs/F	VSD surgical closure for VSD and septal aneurysm	None	Syp. Amoxycillin/Clavulanate 4ml BD	2 days 12 hours	Inj. Cefazolin 250 mg IV TID	34 hours
					Inj. Amikacin 80 mg IV OD	42 hours
66yrs/F	Right laparoscopic nephrectomy	Infected hydroureteronephrosis, UTI	Inj. Ceftriaxone 2 gm IV BD	20 hours	Inj. Ceftriaxone 1 gm IV BD	48 hours
4yrs/M	Bilateral BDG shunt	Pharyngeal colonization with *Pseudomonas aeroginosa*	Inj. Sulbactam/Cefoperazone 400 mg IV TID	6 days 8 hours	Inj. Sulbactam/Cefoperazone 400 mg IV TID	56 hours
			Inj. Amikacin 150 mg IV OD	7 days	Inj. Amikacin 150 mg IV OD	66 hours
63yrs/M	CABG with Mitral Valve Replacement	Urinary Tract Infection (UTI)	Inj Ampicillin 2 gm IV TID	64 hours	Inj. Ceftriaxone 1 gm IV BD	82 hours
			Inj. Gentamicin 60 mg IV TID	16 hours	Inj. Vancomycin 1 gm IV BD	83 hours
62yrs/M	Optical Internal Urethrotomy	Urinary Tract Infection (UTI)	Tab Nitrofurantoin 100 mg BD		Tab Nitrofurantoin 100 mg BD	
1 month 5 days/F	PDA ligation	Blood Stream Infection (BSI)	Syp. Amoxycillin/Clavulanate 1.5ml	12 hours	Inj. Cefazolin 75 mg IV TID	75 hours
					Inj. Amikacin 25 mg IV OD	80 hours

The distribution of the surgeries according to the different categories are 18 of the patients in the sample underwent Coronary Artery Bypass graft (CABG) surgeries. There were 7 paediatric patients and they underwent surgical repair for congenital heart diseases like Tetralogy of Fallot (TOF), Ventricular Septal Defect (VSD), etc. The other adult cardiac surgeries were mainly valve replacement surgeries. The non-cardiac surgeries include mainly laparoscopic procedures such as laparoscopic cholecystectomy, bariatric surgery and gynecologic procedures. The non-cardiac surgeries also included 2 neurosurgeries.

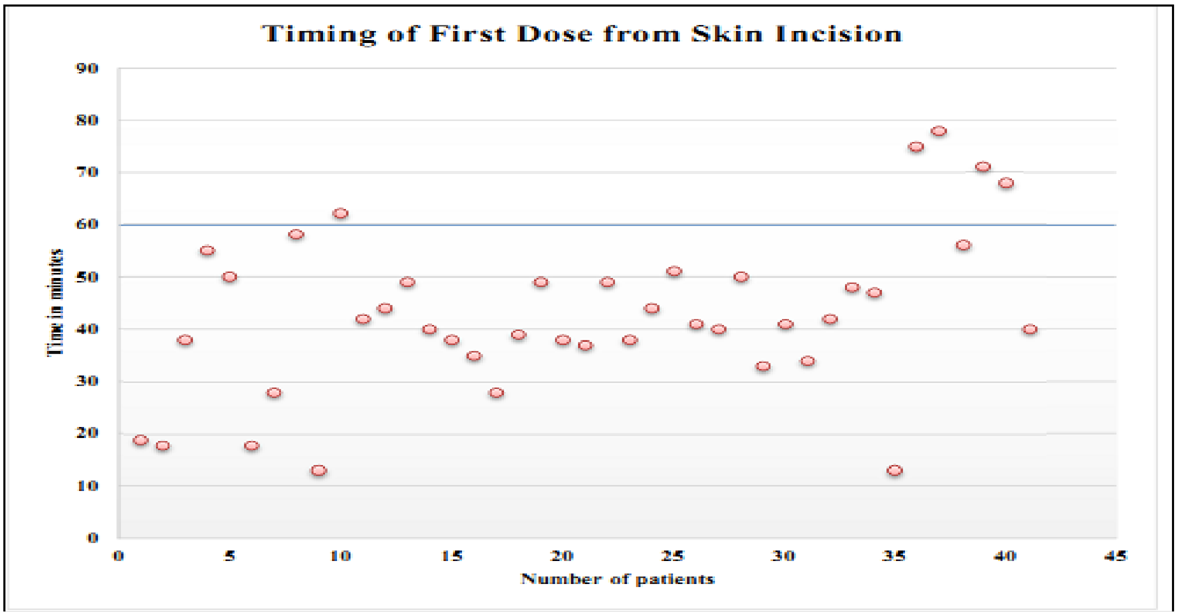


Fig 1: Timing of first Dose from Skin Incision

Figure 1 shows the time lapse in minutes from the first dose of prophylactic antibiotic administered and the skin incision. The guidelines recommend that the first prophylactic dose be administered within 60 minutes from the skin incision to reduce the risk of surgical site infections (SSI). Timing of the first prophylactic antibiotic dose in most of the surgeries (36 of 41 surgeries) was within 60 minutes of the skin incision.

Table 4: Distribution of Surgical Patients According to Prophylactic Antibiotic Duration

Duration of Antibiotic Prophylaxis	*≤24 hours*	*24-48 hours*	*48-72 hours*	*>72 hours*	*Total*
CABGs	**0** (0%)	**1** (5.56%)	**14** (77.78%)	**3** (16.67%)	**18**
Paediatric cardiac surgeries	**1** (14.29%)	**4** (57.14%)	**2** (28.57%)	**0** (0%)	**7**
Other adult cardiac surgeries	**0** (0%)	**0** (0%)	**2** (33.33%)	**4** (66.67%)	**6**
Non-cardiac surgeries	**3** (30.00%)	**4** (40.00%)	**2** (20.00%)	**1** (10.00%)	**10**
TOTAL	**4**	**9**	**20**	**8**	**41**

The duration of antibiotic prophylaxis refers to the duration in which the primary prophylactic antimicrobial agent is actively present in the body. Table-4 shows the distribution of patients in whom the prophylactic antibiotic was stopped within 24 hours, between 24-48 hours, between 48-72 hours and more than 72 hours. The table shows that 4 patients had less than 24 hours of prophylaxis and 9 patients had prophylactic duration up to 24-48 hours. The data shows that 1 of the CABG surgical patients had duration of antibiotic prophylaxis less than 48 hours. 1 non-cardiac surgical patient had less than 24 hours of prophylaxis.

Table 5: Intra-operative redosing of cefazolin in cardiac surgeries.

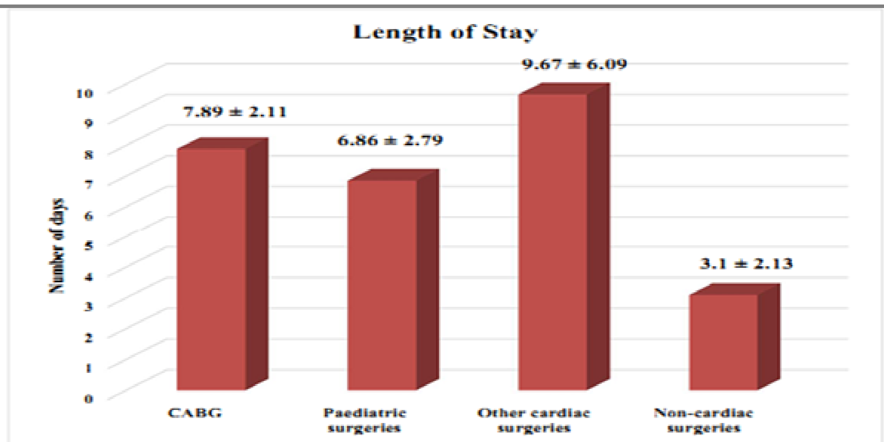
INTRA-OPERATIVE REDOSING IN CARDIAC SURGERIES USING CEFAZOLIN PROPHYLAXIS

Cardiac Surgeries using Cefazolin prophylaxis		*CABG*[b]	*Paediatric surgery*	*Other cardiac surgeries*
Number of surgeries		**18**	**7**	**1**
Mean duration of surgery[a]		**225.06 ± 44.03**	**200.14 ± 55.27**	**160**
Number of surgeries with duration more than 240 minutes		**6**	**2**	**0**
Intra-operative redosing of prophylactic antibiotic	**Yes**	**5**	**0**	**NA**[b]
	No	**1**	**2**	**NA**
Mean duration of surgery when intra-operative redosing was not administered		**283**	**274 ± 36.77**	**NA**

[a]Minutes elapsed between first dose of prophylactic antibiotic and wheel-out from operating room

[b]NA = not applicable; CABG = coronary artery bypass graft

Intra-operative redosing means giving the right number of doses at the right times during the surgical procedure. This depends on the half-life of the antibiotic. Only those surgeries using cefazolin for prophylaxis are considered for intra-operative redosing, due to the half- life of cefazolin being 3-5 hours. The number of cardiac surgeries using cefazolin prophylaxis was 18 CABGs, 7 paediatric cardiac surgeries and one other adult cardiac surgery. In 6 CABGs and 2 paediatric surgeries, the duration of procedure was more than 240 minutes or 4 hours. Intra-operative redosing of cefazolin was given in 5 CABGs and not given in one CABG surgery and 2 paediatric surgeries when duration of procedure was more than 4 hours. 46% of the total number of antimicrobial agents used for surgical prophylaxis was cefazolin. Cefazolin was used either alone, or in combination with other agents such as amikacin or vancomycin. 23% of all the prophylactic antibiotics used were ceftriaxone, which was administered either alone or in combination with vancomycin. Vancomycin and amikacin was used in combination with other agents and formed 14% and 12% of the antibiotics used for prophylaxis, respectively.



[Figure-2]: Duration of stay in the hospital.

Fig 2: Duration of stay in the hospital.

Figure 2 shows the average length of stay (ALOS) in the different categories of surgeries. Length of Stay (LOS) was calculated for each patient as the number of days the patient was in the hospital according to the midnight census. CABG surgical patients stayed in hospital for an average of 7.89 days and paediatric patients stayed in hospital for an average of 6.86 days. The other adult cardiac surgical patients had an average length of stay of 9.67 days and non-cardiac surgical patient stayed 3.1 days in hospital on an average.

4. American Society of Health-System Pharmacists (Ashp) Therapeutic Guidelines

The ASHP guidelines are for surgical antibiotic prophylaxis in all surgeries, cardiac and non-cardiac. In 92.68% of the surgeries the indication for prophylaxis was as per the ASHP guidelines. In few cases such as elective laparoscopic cholecystectomy with no high risk factors for post-operative infections, prophylaxis was not indicated. In 87.80% of surgeries the first prophylactic dose was given within 60 minutes from the skin incision. In 85.37% of the surgeries, the choice of antibiotic given was as per the ASHP guidelines. Dosage of the antibiotic was as per the guideline recommendations in 95.12% of patients. Intra-operative redosing of cefazolin prophylaxis was given in 62.50% of the surgeries longer than 4 hours duration. Prophylactic antibiotic duration (PAD) was as per the guidelines in 7.32% of patients.

Table 6: ASHP Recommended Choice of Antibiotics

Surgery	Given Antibiotic	ASHP Recommended Choice of Antibiotic
Laparoscopic inguinal hernia repair and left orchidectomy	Amoxicillin/Clavulanate	Cefazolin
Laparoscopic myomectomy	Ceftriaxone	Cefazolin
Cervical microdiscectomy with artificial disc replacement	Ceftriaxone	Vancomycin+Cefazolin
Laparoscopic sleeve gastrectomy	Ceftriaxone	Cefazolin
TURP with right hydrocele eversion of sac	Ceftriaxone	Cefazolin
Left retro-sigmoid craniectomy with micro-endoscopic excision	Ceftriaxone	Cefazolin

Table 6 shows the ASHP recommended choice of agent for prophylaxis in the above surgeries. The choice of antibiotic is given as per the local susceptibility patterns of the microorganisms.

5. The Society of Thoracic Surgeons (Sts) Practice Guidelines for Cardiac Surgeries

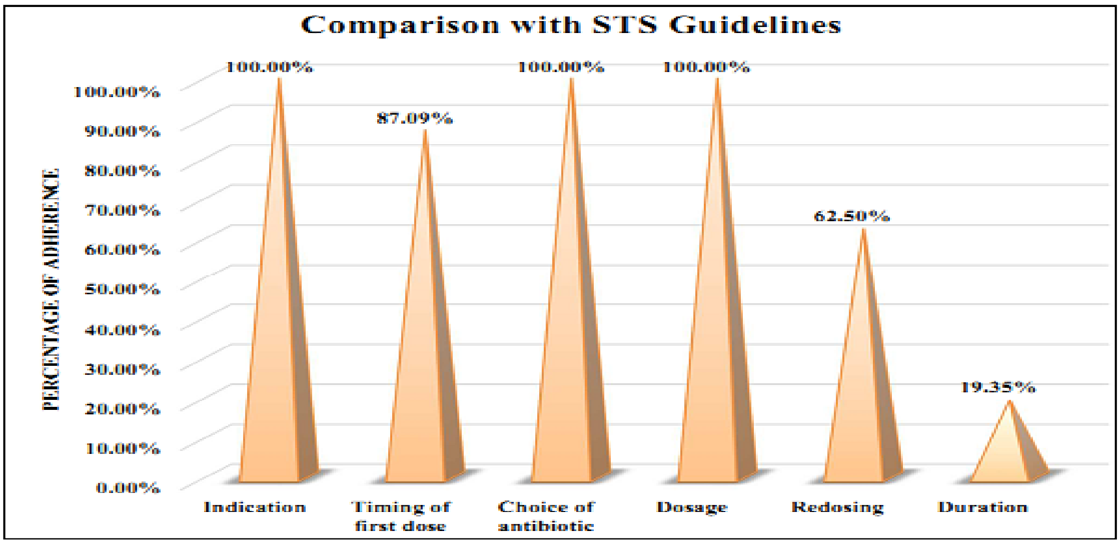


Fig 3: Comparing the Criteria for Rationality with STS Guidelines

The STS guidelines are specifically designed for cardiac surgical antibiotic prophylaxis. Prophylaxis was given as indicated for all the surgeries. In 87.09% surgeries, the initial pre-operative dose of antibiotic was given within 60 minutes of the skin incision. The choice and dosage of prophylactic antibiotic used was consistent with the guidelines in all surgeries. Redosing of cefazolin prophylaxis intra-operatively was done in 62.5% of surgeries where surgery was longer than 4 hours. In 19.35% of patients duration of antibiotic prophylaxis was less than or equal to 48 hours.

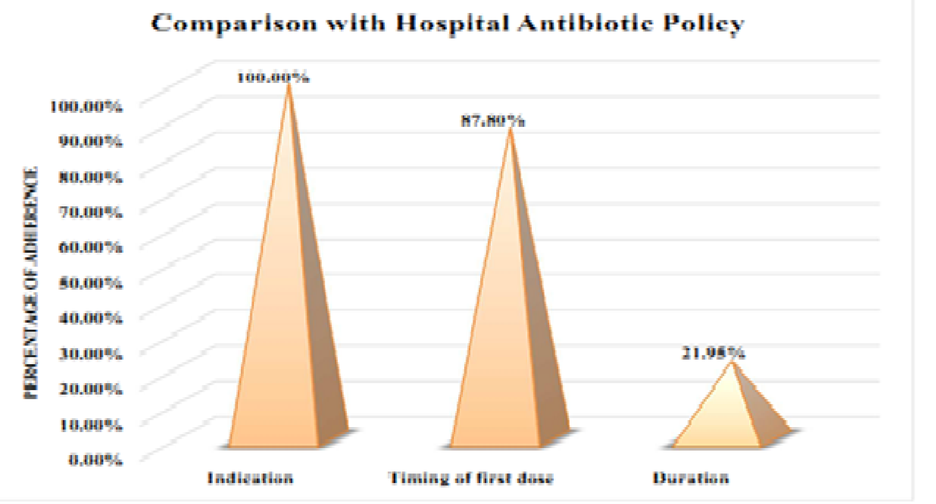


Figure-4 |: Comparing the criteria for rationality with the hospital antibiotic policy.

Fig 4: Comparing the criteria for rationality with the hospital antibiotic policy.

The hospital antibiotic policy includes all the uses of antibiotics. Pertaining to surgical prophylaxis, it lays down guidelines for three parameters which are indication of prophylaxis, timing of first dose and the duration of antibiotic prophylaxis. As per the hospital policy, prophylaxis was given as indicated for all surgeries. The timing of the first prophylactic dose was as per the policy in 87.80% cases. The duration of prophylaxis as per policy guidelines of less than 24 hours for non-cardiac cases and less than 48 hours for cardiac cases was seen in 21.95% of surgeries.

6. Force Field Analysis (Ffa)

Table 7: Positive and negative forces in force field analysis of rationality of antibiotic use in prophylaxis in surgery.

PRIORITY NUMBER	IMPACT	EASEOFCHANGE	+ FORCES (HELPING)[a] →	← -FORCES (HINDERING)[b]	EASE OF CHANGE[c]	IMPACT[d]	PRIORITY NUMBER[e]
7	4	3	Improve team performance of the surgical team	Do not perceive anything wrong with prolonged duration of prophylaxis	4	4	8
6	3	3	Training in effective communication in a critical setting	Lack of institutional controls	4	4	8
8	5	3	Continuous audits and monitoring of antibiotic prophylaxis	Absence of unit or surgery specific antibiotic protocols	5	3	8
7	5	2	Physician advising on a patient specific basis	Limited educational programs	4	3	7
6	5	1	Antibiotic/ formulary restriction and pre-authorization requirement	Difficult to evaluate the end-results or patient outcomes	3	4	7
8	4	4	Physician education and teaching	A "can't hurt, might help" approach or a "just in case" rationale	3	4	7
8	5	3	Distributing an educational handbook	Ambiguity in communication	4	3	7
8	3	5	Providing written standard operating procedures (SOP)	Lack of adequate funds available	2	3	5

[a]Helping forces help to move from the current state to the desired state of rational use.

[b]Hindering forces that hinder this movement to the desired state.

[c]Ease of Change is the ease of increasing helping forces and decreasing hindering forces on a scale of 1-5; 5 = very easy, 1 = very difficult.

[d]Impact of the helping and hindering forces on a scale of 1-5; 5 = very strong, 1 = very weak.

[e]Priority Number is the sum of the two values.

7. Highest ranking of helping forces according to priority number

- Continuous audits and monitoring of antibiotic prophylaxis
- Physician education and teaching
- Distributing an educational handbook
- Providing written standard operating procedures (SOP)
- Implementation of a Surgical Safety Checklist

8. Highest ranking of hindering forces according to priority number

- Do not perceive anything wrong with prolonged duration of prophylaxis
- Lack of institutional controls
- Absence of unit or surgery specific antibiotic protocols
- Resistance to change from current practice
- Not checking the type of procedure or patient risk factors like obesity

The force field analysis shows that interventions such as continuous audits, physician education and providing written standard operating procedures to be followed will help to reach the desired state of rational antibiotic use in surgical prophylaxis.

9. Cause and Effect Diagram

Cause and effect diagram is one of the seven tools of quality, it shows the relationship of all factors (causes) that lead to the given situation (effect). It identifies major causes and breaks them down into sub-causes and further sub-divisions (if any). It is usually preceded by cause-and-effect analysis. Also called fishbone diagram (because of its resemblance to a fish skeleton) or Ishikawa diagram, after its inventor Dr. Kaoru Ishikawa (1915-89) of Tokyo's Mushasi Institute.

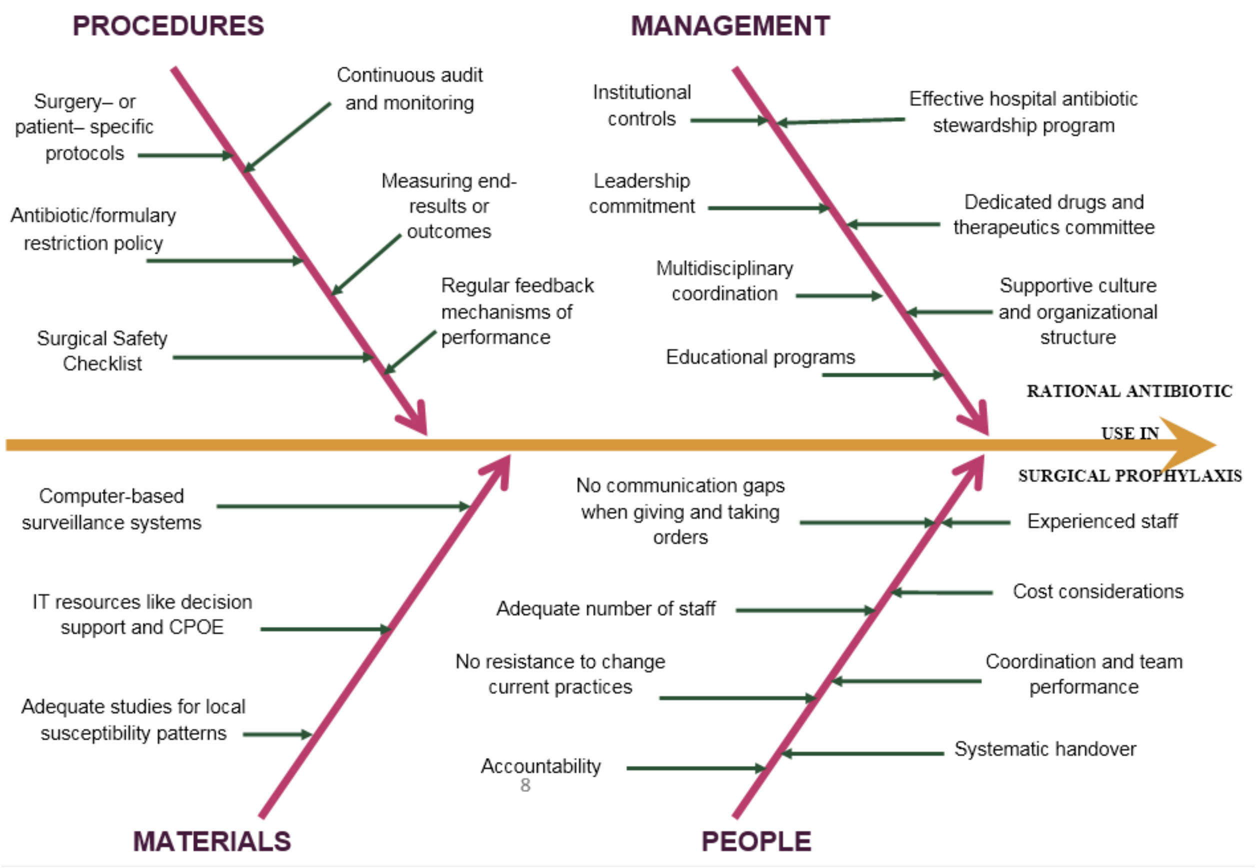


Fig 5: Cause and Effect Analysis of Rational Antibiotic Use in Surgical Prophylaxis

10. Discussion

After comparison of the current practices with the international ASHP and STS guidelines, it was found that the following parameters had highest adherence to the recommendations. The highest conformance to the ASHP guidelines was found in case of the indication of use of antibiotic prophylaxis (92.68%), the dosage of antibiotic agent (95.12%) and the timing of the first pre-operative dose (87.80%). The conformance was observed to be least in the duration of antibiotic prophylaxis (7.32%). In case of the STS guidelines, highest adherence to the recommendations was seen in the choice of prophylactic agent (100%) and the timing of the first pre-operative dose of antibiotic (87.09%). The duration of antibiotic prophylaxis was only 19.35% adherent to the guidelines. On comparison with the hospital antibiotic policy, 100% conformance was seen to the indication of use, timing of first dose was as per policy in 87.80% cases and duration of antibiotic prophylaxis was as per policy in 21.95% of patients. It was found in the study that the hospital antibiotic policy does not include all the parameters for rational use of antibiotics in surgical prophylaxis as seen in the ASHP and STS guidelines. Hence, these must also be added to the current policy.

The first principle of antibiotic prophylaxis in surgery is the administration of the first dose of antibiotic within 60 minutes of the skin incision. If it is administered more than 60 minutes from the incision, the concentration of the drug in the wound tissue during the time the wound remains open throughout the surgery will be reduced, which makes it likely for pathogens to infect the surgical site. In this study, 88.46% of the surgeries followed the recommendations with the first dose being within 60 minutes of the incision.

The most controversial principle of antibiotic prophylaxis in surgery is the duration of prophylaxis. While in the ASHP guidelines, it is recommended for any type of surgery including cardiac surgeries for duration of prophylaxis to be less than 24 hours, the STS guidelines state that it should be less than 48 hours in cardiac surgery and less than 24 hours for other surgeries. In this study most of the surgical patients had prophylactic antibiotic administration for more than 48 hours indicating that this is the important area requiring interventions for achieving the stated objective of appropriate antibiotic use in prophylaxis. This longer duration of prophylaxis is due to a comfort zone, where it is falsely assumed that the longer the duration, the lesser the chance of the patient getting an infection. Several studies have proven that there is no difference in the rate of surgical site infections (SSI) when the duration is either less than 24 hours or more than 24 hours. Hence, the ASHP guideline recommends that it is better if duration of prophylaxis be less than 24 hours for all surgeries including cardiac surgeries. However, the STS guideline allows an extension to 48 hours in case of cardiac surgeries. This is because cardiac patients are more prone to develop surgical site infections and other complications due to the nature of their surgery, the use of cardiopulmonary bypass and the more prolonged duration of the surgery, lasting sometimes more than 4 hours.

In the case of insertion of prosthetic valves as in valve replacement surgeries, the complications are more severe if the prosthetic valve is infected, since the foreign body is difficult to remove. These patients were seen to have prolonged duration of antibiotic prophylaxis. Also, being a sicker group of patients, these patients mostly suffered from other complications too and had longer duration of hospital stay. There are other independent risk factors for post-operative surgical site infections such as pre-operative hospitalization for an extended number of days, use of previous antibiotics, recent infections, etc. Also, the present scenario in the local conditions is different from that taken into consideration in the international guidelines. Hence the study of rationality of antibiotic use requires more consideration of the local population and microbiological characteristics.

11. Recommendations

From the analysis of this study, it is recommended that interventions such continuous monitoring of antibiotic use, antibiotic restriction policies, automatic dose stopping forms, computer surveillance of local infectious and microbiological patterns, etc. are useful for the rational use of antibiotics in surgical prophylaxis. Distribution of an educational handbook and standard operating procedures to be followed can help to bring about a reduction in the duration of prophylaxis also.

12. Conclusion

All the criteria for rationality of antibiotic use in surgical prophylaxis have been in high conformance to the guidelines and the hospital policy except for the duration of prophylaxis. The study also identified that all the criteria for rational antibiotic use in surgical prophylaxis as stated by the international guidelines have not been included in the hospital antibiotic policy and should be included.

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